UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/866,307 | 05/25/2001 | Lawrence P. Wackett | 110.00440102 | 4705 |

26813 7590 07/15/2003

MUETING, RAASCH & GEBHARDT, P.A.
P.O. BOX 581415
MINNEAPOLIS, MN 55458

| EXAMINER | |
|---|---|
| HUTSON, RICHARD G | |
| **ART UNIT** | **PAPER NUMBER** |
| 1652 | 12 |

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/866,307 | WACKETT ET AL. | |
| | Examiner | Art Unit | |
| | Richard G Hutson | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *25-30 and 35-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-29,35-40,42-44,46-48 and 50* is/are rejected.

7)☐ Claim(s) *30, 41, 45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Applicants amendment of the specification, cancellation of claims 2-11, 23, 24, and 31-34, amendment of claims 25 and 30 and addition of new claims 35-50, Paper No. 11, 4/28/2003, is acknowledged. Claims 2-11 and 25-30 and 35-50 are at issue and are present for examination. Applicants' arguments filed on 4/28/2003, Paper No. 11, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### *Information Disclosure Statement*

As stated previously, applicants filing of an information disclosure statement filed on 5/25/2001 is acknowledged. Applicants reference to "the information disclosure statement submitted on August 23, 2002." is unclear as no such IDS is found in the application. A preliminary amendment filed on August 23, 2002 is in the application file, however the only IDS which is currently in the file is that filed on 5/25/2001.

### *Specification*

The disclosure is objected to because of the following informalities:

As previously stated, Figure 9 comprises a comparison of **six** different amino acid sequences from **six** different types of bacteria as indicated in the description of Figure 9. The description of figure 9 also recites "SEQ ID NOs: 12-16". There is no indication as to which "SEQ ID NO" is associated with which sequence from which

bacteria and **further SEQ ID NOS 12-16 comprise only five sequences, not six as are listed in the figure**.

In response to this previous objection to the specification applicants have amended the description of Figure 9 to specify which SEQ ID NO: is associated with each bacterial sequence, however, applicants amendment indicates that the sequence identifier for Pseudomonas sp. Strain ADP is SEQ ID NO: 16 and the sequence identifier for Clavibacter (Clav.) is SEQ ID NO: 16. Appropriate explanation and/or amendment is requested.

Appropriate correction is required.

### *Claim Objections*

Claims 30, 41 and 45 are objected to because of the following informalities:

Claims 30, 41 and 45 depend from rejected claims.

Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-29, 35-40, 42-44, 46-48 and 50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 25-30. In response to this rejection applicants have amended claims 29 and 30 and traverse the rejection as it applies to amended claims 29-30. Newly added claims 35-40, 42-44, 46-48 and 50 are included in this rejection for the same reasons previously stated for claims 29-30. Applicants argument with respect to claims 29-30 is also applied to considered with respect to newly added claims 35-40, 42-44, 46-48 and 50 below.

Applicants traverse the rejection on the basis that by amendment applicants have limited the genus of those proteins used in the genus of methods claimed by claims 25-29 to those proteins which are encoded by a nucleic acid capable of hybridizing under high stringency conditions as defined in the claims to SEQ ID NO: 1. Applicants further point out that the method of claim 30 is drawn to a method of using the proteins having the amino acid sequence of SEQ ID NOs: 5, 6, and 22-26. Thus applicants submit that the proteins of claims 25-30 are described. While applicants argument is persuasive with respect to claim 30, applicants argument is not found persuasive with respect to claims 25-29 on the basis that while applicants have amended claims 25-29 to include the structural limitation of the proteins used in the claimed methods, applicants have not disclosed a correlation between the proteins encompassed by this structural limitation (i.e. those proteins having the amino acid sequence of SEQ ID NOs 5, 6 and 22-26) and the claimed newly added functional limitation(s) (i.e. those atrazine chlorohydrolases

having an altered catalytic rate as quantified by $k_{cat}$ and $K_M$ , altered substrate range, altered substrate preference, altered activity in aqueous solutions, altered stability in solvents, altered active temperature range, altered salt concentrations for enzymatic activity, altered pH for enzymatic activity and improved activity in a soil environment).

Applicants further argue that according to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112 first paragraph, it may be shown that "an invention is complete by disclosure of sufficiently detailed relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure *or some combination of such characteristics*". While it is acknowledged that claim 25 has both structural characteristics and functional characteristics, there is no teaching of any relationship between the defined structural characteristics and the various different functional characteristics such that the claimed genus of methods of use is not defined based on inadequate description of the genus of proteins having the claimed structural and various functional characteristics. It is acknowledged that applicants teach 7 species of proteins (i.e. SEQ ID NOs: 5, 6, and 22-26), however how each of the se species relates to the functional characteristics of the proteins of the claimed method is unclear, thus applicants have not adequately described the genus of methods of use of such a genus of atrazine chlorohydrolase enzymes.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 25-29, 35-40, 42-44, 46-48 and 50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a sample comprising an s-triazine-containing compound comprising adding a composition to a sample comprising an s-triazine-containing compound, wherein the composition comprises a protein of SEQ ID NO: 2, 5, 6 or 22-26, does not reasonably provide enablement for any method of treating a sample comprising an s-triazine-containing compound comprising adding a composition to a sample comprising an s-triazine-containing compound, wherein the composition comprises a protein encoded by a nucleic acid which hybridizes under the specified high stringency conditions wherein the protein has a altered catalytic activity relative to the protein of SEQ ID NO: 2, wherein the altered catalytic activity is selected from the group consisting of altered catalytic rate as quantified by kcat and KM , altered substrate range, altered substrate preference, altered activity in aqueous solutions, altered stability in solvents, altered active temperature range, altered salt concentrations for enzymatic activity, altered pH for enzymatic activity and improved activity in a soil environment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 25-29, 35-40, 42-44, 46-48 and 50 are so broad as to encompass any method of treating a sample comprising an s-triazine-containing compound comprising adding a composition to a sample comprising an s-triazine-containing compound, wherein the composition comprises a protein encoded by a nucleic acid which hybridizes under the specified high stringency conditions wherein the protein has a altered catalytic activity relative to the protein of SEQ ID NO: 2, wherein the altered catalytic activity is selected from the group consisting of altered catalytic rate as quantified by $k_{cat}$ and $K_M$, altered substrate range, altered substrate preference, altered activity in aqueous solutions, altered stability in solvents, altered active temperature range, altered salt concentrations for enzymatic activity, altered pH for enzymatic activity and improved activity in a soil environment.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of enzymes broadly encompassed by the claims, including all enzymes having the structural relationship to SEQ ID NO: 2 as dictated by the claim, wherein said enzyme is mutated such that it has

an altered catalytic activity selected from the group consisting of altered catalytic rate as quantified by $k_{cat}$ and $K_M$, altered substrate range, altered substrate preference, altered activity in aqueous solutions, altered stability in solvents, altered active temperature range, altered salt concentrations for enzymatic activity, altered pH for enzymatic activity and improved activity in a soil environment. While the methods encompassed by the rejected claims place structural limitations on the mutant enzymes used in the claimed methods, applicants have not enabled the claims with respect to how to make the claimed mutant enzymes. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited the atrazine degrading enzyme having the amino acid sequence of SEQ ID NO: 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to

modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all methods of use of the claimed mutant atrazine degrading enzymes having the amino acid sequence of SEQ ID NO: 2and having the specified alterations in catalytic activity, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting atrazine degrading activity or those regions responsible for such alterations in atrazine catalytic activity selected from the group consisting of altered catalytic rate as quantified by $k_{cat}$ and $K_M$, altered substrate range, altered substrate preference, altered activity in aqueous solutions, altered stability in solvents, altered active temperature range, altered salt concentrations for enzymatic activity, altered pH for enzymatic activity and improved activity in a soil environment ; (B) the general tolerance of atrazine degrading enzymes to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a atrazine degrading enzyme with an expectation of obtaining the desired altered catalytic activity; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the atrazine degrading activity while simultaneously altering this activity such as altering the catalytic rate as quantified by $k_{cat}$ and $K_M$, altering the substrate range, altering the substrate preference, altering the activity in aqueous solutions, altering the stability in solvents, altering the

active temperature range, altering the salt concentrations for enzymatic activity, altering the pH for enzymatic activity and improving the activity in a soil environment as claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those methods of use of the claimed mutant atrazine degrading enzymes.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the claimed method of use of the claimed mutant atrazine degrading enzymes. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those enzymes, for use in the claimed methods, which have the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
July 11, 2003